ORIGINAL ARTICLE

DOI: 10.4274/gulhane.galenos.2026.77675
Gulhane Med J

Impact of maternal thyroid autoimmunity on fetal neurosonographic parameters and cerebral hemodynamics

Hale Özer Çaltek, Cansu Tekin Pişirici, Işıl Turan Bakırcı, Hakan Erenel

University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital, Department of Perinatology, İstanbul, Türkiye

Cite this article as: Özer Çaltek H, Tekin Pişirici C, Turan Bakırcı I, Erenel H. Impact of maternal thyroid autoimmunity on fetal neurosonographic parameters and cerebral hemodynamics. *Gulhane Med J.* [Epub Ahead of Print]

Date submitted:
12.04.2026
Date accepted:
22.09.2026
Epub:
27.10.2026

Corresponding Author:
Hale Özer Çaltek, MD, University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital, Department of Perinatology, İstanbul, Türkiye

ORCID:
orcid.org/0000-0002-1433-6942

Keywords: Maternal hypothyroidism, thyroid autoimmunity, fetal neurosonography, middle cerebral artery Doppler, cerebral hemodynamics, pregnancy

ABSTRACT

Aims: Maternal thyroid dysfunction and thyroid autoimmunity have been associated with adverse pregnancy outcomes, yet their effects on fetal brain development and cerebral circulation remain unclear. This study aimed to evaluate the association between maternal thyroid status, including thyroid autoimmunity, and fetal neurosonographic parameters and cerebral hemodynamics in the second trimester. To our knowledge, data evaluating both fetal neurosonographic parameters and cerebral Doppler findings in this context are limited.

Methods: In this prospective observational study, 118 singleton pregnancies between 20 and 24 weeks of gestation were evaluated. Participants were stratified into three groups: Hypothyroid with thyroid autoimmunity, hypothyroid without autoimmunity, and euthyroid controls. Standardized fetal biometric and detailed neurosonographic measurements were obtained, and the middle cerebral artery pulsatility index (MCA-PI) was assessed. Associations between maternal thyroid status and fetal outcomes were evaluated, with adjustment for gestational age, maternal body mass index, and parity.

Results: A total of 118 pregnancies were included (mean gestational age: 21.99±1.22 weeks; 52% male fetuses). Most fetal biometric and neurosonographic parameters were comparable across groups (all p>0.05). Although corpus callosum length (p=0.022) and thalamic diameter (p=0.013) differed in unadjusted analyses, these differences were not sustained after adjustment. In contrast, fetuses of mothers with hypothyroidism and thyroid autoimmunity had significantly lower MCA-PI values compared with euthyroid controls (B=-0.33, p=0.001). This finding remained significant after adjustment for potential confounders. No independent associations were observed between maternal thyroid status and structural fetal brain parameters.

Conclusions: Maternal hypothyroidism with thyroid autoimmunity is associated with lower fetal MCA-PI values in the second trimester, suggesting subtle alterations in fetal cerebral hemodynamics, even in the absence of structural brain differences. These findings may have implications for understanding the effects of maternal thyroid dysfunction on fetal circulation during pregnancy.

Copyright© 2026 The Author(s). Published by Galenos Publishing House on behalf of University of Health Sciences Türkiye, Gülhane Faculty of Medicine.
This is an open access article under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 (CC BY-NC-ND) International License.

Introduction

During pregnancy, particularly in the first trimester, thyroid hormones play a critical role in fetal brain growth and maturation. At this stage, the fetus is highly dependent on maternal thyroxine, as fetal thyroid function is not yet functionally mature. Although the fetal hypothalamic-pituitary-thyroid axis is largely established by the first trimester (1), the fetus remains dependent on maternal thyroid hormones until approximately 18-20 weeks, making this period a critical window for neurodevelopment (2).

Maternal hypothyroidism during early pregnancy has been associated with impaired fetal brain development, and delayed or insufficient thyroid hormone replacement may result in irreversible neurodevelopmental deficits (3). Thyroid dysfunction is common during pregnancy, with both overt and subclinical hypothyroidism affecting a substantial proportion of women. At the same time, thyroid autoimmunity is also frequently observed and has been associated with adverse reproductive outcomes (4).

Although previous studies have demonstrated the importance of maternal thyroid function in fetal neurodevelopment, data on its association with detailed fetal brain structures and cerebral hemodynamics assessed by prenatal ultrasound remain limited. In particular, the relationship between thyroid autoimmunity and fetal brain measurements remains unclear. Moreover, the impact of maternal thyroid autoimmunity on fetal cerebral Doppler parameters, particularly middle cerebral artery pulsatility index (MCA-PI), remains inadequately investigated.

Maternal thyroid autoimmunity has been associated with adverse perinatal outcomes, including miscarriage and preterm birth. It has also been linked to offspring neurodevelopmental outcomes, although the underlying mechanisms remain unclear (2,5). Whether these associations are reflected in prenatal fetal brain measurements or cerebral Doppler parameters has not been well established.

Therefore, this study aimed to evaluate the association between maternal thyroid status, including thyroid autoimmunity, and both fetal neurosonographic parameters and cerebral hemodynamics assessed by MCA Doppler in the second trimester. We hypothesized that maternal thyroid autoimmunity may affect fetal cerebral blood flow, even in pregnancies receiving appropriate thyroid hormone replacement therapy.

Methods

Study design and setting

This prospective observational study was conducted between October 1, 2025, and March 1, 2026, after approval from the Institutional Ethics Committee of University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital (approval number: E-96317027-514.10, date: 16/09/2025). Written informed consent was obtained from all participants before participation in the study. The study protocol conforms to the ethical guidelines of the Declaration of Helsinki (1975), as revised in 2013, and was approved by the Institutional Ethics Committee of University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital.

Participants

It included pregnant women who presented for a detailed fetal anatomical ultrasound examination between 20 and 24 gestational weeks. The 20-24-week interval was selected because it corresponds to the routine detailed fetal anatomical and neurosonographic examination in our perinatology clinic, which is often the first standardized opportunity for fetal biometric, neurosonographic, and cerebral Doppler assessment. This timing allowed us to evaluate whether differences related to maternal thyroid status could be detected at the usual referral period for detailed fetal assessment, before the possible influence of late-pregnancy complications.

Participants were stratified into three groups according to maternal thyroid function and autoimmunity status. The first group consisted of pregnant women with hypothyroidism secondary to Hashimoto's thyroiditis diagnosed before pregnancy, who were under routine follow-up at our clinic. The diagnosis had been previously established based on clinical evaluation and documented positivity for anti-thyroid peroxidase (anti-TPO) and/or anti-thyroglobulin (anti-TG) antibodies, and, when available, cytological evidence of lymphocytic infiltration (6). The second group included hypothyroid pregnant women without evidence of thyroid autoimmunity, characterized by elevated thyroid-stimulating hormone (TSH) levels in the absence of detectable thyroid autoantibodies. Both hypothyroid groups were receiving levothyroxine replacement therapy during pregnancy, and thyroid function tests were within normal reference ranges at the time of the detailed ultrasound examination. The third group consisted of euthyroid pregnant women with normal thyroid function tests and negative thyroid autoantibodies.

Women in both hypothyroidism groups had documented hypothyroidism before pregnancy and during the first trimester and subsequently achieved biochemical euthyroidism under levothyroxine treatment by the time of fetal ultrasound assessment. Therefore, normal thyroid function at 20-24 weeks reflected treatment response rather than the absence of thyroid dysfunction earlier in pregnancy.

Maternal age was restricted to a relatively narrow range (18-34 years) as part of the inclusion criteria to minimize its potential confounding effect. Multiple gestations, fetal growth restriction, women with known chronic systemic diseases, smokers, preeclampsia or gestational diabetes mellitus, pregnancy-induced transient hypothyroidism, and fetuses with known genetic or structural abnormalities were excluded from the study, as these conditions may independently affect fetal neurodevelopment and cerebral hemodynamics. Umbilical and

uterine artery Doppler assessments were performed as part of routine clinical evaluation and were within normal limits in all included pregnancies. Therefore, these parameters were not included as study variables and were not incorporated into the statistical analysis.

Assessment of thyroid function

Thyroid function and autoantibody levels were assessed during the first trimester. According to national guidelines, hypothyroidism was defined as a TSH level > 2.5 mIU/L (7). Thyroid autoimmunity was determined as anti-TPO levels > 34 IU/mL and/or anti-TG levels > 40 IU/mL. Autoantibody status was interpreted as positive or negative according to these cut-off values and was used to classify participants rather than as a continuous variable. These measurements were used to confirm and standardize previously established diagnoses.

Ultrasound evaluation

All ultrasound examinations were performed by the same maternal-fetal medicine specialist using a high-resolution ultrasound system (Arietta 850, Hitachi Medical Systems, Tokyo, Japan) equipped with a 3.5 MHz transabdominal probe. Standard fetal biometric measurements (biparietal diameter, head and abdominal circumference, and femur length), detailed fetal brain measurements (ventricular posterior length, nuchal fold thickness, cavum septi pellucidi, corpus callosum length, corpus callosum body thickness, and thalamic diameter), and MCA-PI were performed in accordance with the recommendations of the International Society of Ultrasound in Obstetrics and Gynecology (8,9). MCA-PI was measured from the proximal third of the vessel near its origin from the circle of Willis, with the angle of insonation maintained between 0° and 30° (10). For each fetus, MCA-PI was calculated as the mean of at least three consecutive waveforms of adequate quality. The examiner was blinded to the maternal thyroid diagnosis and thyroid autoantibody status at the time of the examination.

Statistical Analysis

All statistical analyses were performed using R statistical software version 4.4.2 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were summarized as mean ± standard deviation, whereas categorical variables were presented as counts and percentages.

Comparisons of maternal and fetal characteristics across maternal thyroid status groups (normal thyroid function, hypothyroid antibody-positive, and hypothyroid antibody-negative) were performed using appropriate statistical tests based on the variable type. Categorical variables were compared using Fisher's exact test, while continuous variables were compared using the Kruskal-Wallis rank-sum test, as normality assumptions were not consistently met.

To better evaluate the association between maternal thyroid status and fetal brain measurements, multivariable linear regression models were constructed. Each fetal brain measurement (ventricular posterior, nuchal fold thickness, cavum septi pellucidi, corpus callosum length, corpus callosum body thickness, thalamic diameter, and middle cerebral artery Doppler values) was analyzed as a dependent variable. Maternal thyroid status was included as the primary independent variable, and models were adjusted for gestational age at examination, parity, and maternal body mass index (BMI) to account for potential confounding effects.

Regression results were reported as unstandardized regression coefficients (B), standard errors, t-statistics, and p-values. A two-sided p-value <0.05 was considered statistically significant.

A post-hoc power analysis based on the primary endpoint (MCA-PI) demonstrated that the study had sufficient statistical power (>80%) to detect moderate-to-large effect sizes; however, it may have been underpowered to detect small effect sizes.

Results

Baseline characteristics

A total of 118 pregnant women were included in the analysis. The mean maternal BMI was 30.35±4.30 kg/m², and the mean gestational age at examination was 21.99±1.22 weeks. Most participants were euthyroid (60%), while 21% had hypothyroidism with thyroid autoimmunity and 19% had hypothyroidism without autoimmunity. Overall fetal biometric and neurosonographic measurements were within expected ranges for gestational age (Table 1).

Comparisons between maternal thyroid status groups

Maternal and fetal characteristics according to thyroid status are presented in Table 2. Gravidity differed significantly across the groups (Fisher's exact test, p=0.008), and this difference remained significant after false discovery rate (FDR) correction (q=0.041). Similarly, parity distribution also showed a significant difference between groups (p=0.011, q=0.041).

Maternal BMI varied significantly among the groups, with higher values observed in both hypothyroid groups compared with the euthyroid group (Kruskal-Wallis test, p<0.001, q=0.008). In contrast, gestational age at examination (p=0.052, q=0.12) and fetal sex distribution (p=0.085, q=0.20) were comparable across groups.

Most fetal biometric and neurosonographic parameters were comparable across groups, including biparietal diameter, head circumference, abdominal circumference, femur length, ventricular posterior width, nuchal fold thickness, cavum septi pellucidi, and corpus callosum body thickness, with no statistically significant differences observed (all p>0.05 and q>0.05).

Table 1. Baseline characteristics and fetal measurements of the study population

Characteristic	**n=118[1]**
Gravida	**n (%)**
1	48 (41)
2	37 (31)
3	17 (14)
4	9 (7.6)
5	5 (4.2)
7	2 (1.7)
Parity	**n (%)**
0	50 (42)
1	49 (42)
2	11 (9.3)
3	6 (5.1)
4	2 (1.7)
Maternal BMI, kg/m^2, mean ± SD	30.35±4.30
Maternal thyroid status	**n (%)**
Euthyroid	71 (60)
Hypothyroid antibody+	25 (21)
Hypothyroid antibody-	22 (19)
Gestational age (weeks), mean ± SD	21.99±1.22
Fetal sex	**n (%)**
Female	56 (47)
Male	62 (53)
Fetal measurements	**Mean ± SD**
BPD (mm)	52.73±4.76
HC (mm)	197.65±18.88
AC (mm)	170.15±17.19
FL (mm)	37.60±3.95
Ventricular posterior (mm)	6.10±1.11
Nuchal fold (mm)	4.46±0.81
CSP (mm)	4.62±1.08
Corpus callosum length (mm)	22.89±3.76
Corpus callosum body (mm)	2.05±1.08
Thalamus (mm)	11.67±1.68
MCA-PI	1.58±0.41

[1]: n (%); mean ± standard deviation, BMI: Body mass index, BPD: Biparietal diameter, mm: Millimeter, HC: Head circumference, AC: Abdominal circumference, FL: Femur length, VP: Ventricule posterior, NF: Nuchal fold, CSP: Cavum septi pellucidi, MCA-PI: Middle cerebral artery-pulsatility index, SD: Standard deviation

Among fetal brain parameters, corpus callosum length showed a nominally significant difference (p=0.022); however, this did not remain significant after FDR correction (q=0.058). In contrast, thalamic diameter differed significantly between groups (p=0.013, q=0.041), with lower mean values observed in the hypothyroid antibody-negative group.

MCA-PI measurements also demonstrated a clear group difference (p<0.001, q=0.008), with the lowest values in the hypothyroid antibody-positive group and higher values in the euthyroid group.

Multivariable regression analysis

Multivariable linear regression analyses evaluating the independent association between maternal thyroid status and fetal outcomes are presented in Table 3.

Multivariable linear regression analyses showed that, after adjusting for gestational age, maternal BMI, and parity, maternal thyroid status was not independently associated with most fetal brain measurements.

No significant associations were observed for ventricular posterior length, cavum septi pellucidi, corpus callosum length and body thickness, or thalamic diameter (all p>0.05), with confidence intervals (CIs) crossing zero, indicating a lack of statistically reliable effects.

In contrast, a significant association was identified for MCA-PI values. Fetuses of mothers with hypothyroid antibody positivity had lower MCA-PI values compared with those in the euthyroid group [B=-0.334, 95% CI (-0.527, -0.142), p<0.001], indicating a potential difference in fetal cerebral hemodynamics associated with maternal thyroid autoimmunity.

Additionally, a borderline significant decrease in nuchal fold thickness was observed in the hypothyroid antibody-negative group [B=-0.407, 95% CI (-0.811,-0.003), p=0.048]. However, as the CI approached zero, this finding should be interpreted with caution.

Discussion

In this study, we evaluated the association between maternal thyroid function and thyroid autoimmunity with fetal neurosonographic parameters and cerebral hemodynamics in the second trimester. The main findings of our study can be summarized as follows: first, overall fetal biometric measurements were not significantly affected by maternal thyroid status; second, although some fetal brain parameters, including corpus callosum length and thalamic diameter, differed between groups in unadjusted analyses, these associations were not sustained after adjustment for confounding factors; and third, MCA-PI values were significantly lower in fetuses of mothers with hypothyroidism and thyroid autoimmunity, even after adjustment for potential confounders.

Our findings are partially consistent with previous reports evaluating fetal brain structures in pregnancies complicated by maternal hypothyroidism and thyroid autoimmunity. Torun et al. (11) reported lower thalamic measurements and posterior ventricular length in fetuses of mothers with hypothyroidism and thyroid autoimmunity. Similarly, in our cohort, differences in corpus callosum length and thalamic diameter were observed in

Table 2. Comparison of characteristics according to maternal thyroid status

Characteristic	Normal n=71[1]	Hypothyroid antibody+ n=25[1]	Hypothyroid antibody- n=22[1]	p-value[2]	q-value[3]
Gravida	**n (%)**	**n (%)**	**n (%)**	0.008	0.041
1	24 (34)	8 (32)	16 (73)		
2	22 (31)	12 (48)	3 (14)		
≥3	25 (35)	5 (20)	3 (14)		
Parity	**n (%)**	**n (%)**	**n (%)**	0.011	0.041
0	26 (37)	8 (32)	16 (73)		
1	30 (42)	15 (60)	4 (18)		
≥2	15 (21)	2 (8.0)	2 (9.1)		
BMI (mean ± SD)	29.14±4.10	32.44±3.60	31.87±4.42	<0.001	0.008
Gestational week (mean ± SD)	22.13±1.18	22.07±1.11	21.45±1.34	0.052	0.12
Fetal sex	**n (%)**	**n (%)**	**n (%)**	0.085	0.2
Female	38 (54)	7 (28)	11 (50)		
Male	33 (46)	18 (72)	11 (50)		
Fetal measurements	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**		
BPD	52.94±4.34	53.54±5.26	51.13±5.30	0.11	0.2
HC	198.51±19.39	200.24±18.14	191.95±17.67	0.12	0.2
AC	171.76±14.57	167.76±24.68	167.68±14.83	0.6	0.6
FL	37.86±3.56	38.26±4.30	36.01±4.49	0.10	0.2
VP	6.03±1.14	6.34±1.18	6.06±0.90	0.3	0.3
NF	4.60±0.78	4.35±0.81	4.13±0.81	0.11	0.2
CSP	4.60±0.93	4.77±1.11	4.52±1.46	0.2	0.3
CC-length	23.55±2.97	22.80±4.70	20.87±4.27	0.022	0.058
CC-body	2.14±1.32	1.98±0.56	1.86±0.43	0.5	0.5
Thalamus	11.93±1.71	11.78±1.60	10.67±1.32	0.013	0.041
MCA-PI	1.67±0.36	1.34±0.30	1.55±0.55	<0.001	0.008

[1]: n (%); mean ± SD, [2]: Fisher's exact test, Kruskal-Wallis rank sum test, [3]: Benjamini & Hochberg correction for multiple testing, BMI: Body mass index, BPD: Biparietal diameter, HC: Head circumference, AC: Abdominal circumference, FL: Femur length, VP: Ventricule posterior, NF: Nuchal fold, CSP: Cavum septi pellucidi, CC: Corpus callosum, MCA-PI: Middle cerebral artery-pulsatility index, SD, Standard deviation

unadjusted analyses but were not maintained after adjustment. These findings indicate that maternal thyroid status was not independently associated with fetal brain structural parameters after adjustment, and that the observed unadjusted differences were likely driven by confounding maternal characteristics. In our study, maternal BMI and parity also differed significantly between groups, as reported by Torun et al. (11), and may have acted as confounders in the observed associations. Although Torun et al. (11) reported that lower thalamic measurements persisted within overweight and obese subgroups, the absence of multivariable adjustment in that study limits the ability to exclude residual confounding by other maternal and clinical factors.

Although prenatal neurosonographic studies are limited, postnatal imaging studies also support our findings. In the CATS III follow-up study, no significant differences in global brain volumes were observed according to maternal thyroid status and levothyroxine treatment during pregnancy (12). Similarly, Korevaar et al. (13) found no significant association between maternal TSH levels and child brain morphology. These findings support our observation that differences in fetal brain measurements did not persist after adjustment for potential confounders.

The main Doppler finding of our study was the reduction in MCA-PI values in fetuses of mothers with hypothyroidism and thyroid autoimmunity. When evaluated according to gestational age-specific reference percentiles, MCA-PI values in the euthyroid group ranged from the 11th to the 96th percentile, whereas values in the hypothyroid antibody-positive and antibody-negative groups ranged from the 1st to the 62nd percentile and from the 1st to the 99th percentile, respectively. These findings suggest a downward shift in fetal cerebral Doppler indices in both hypothyroid groups, although the association remained independently significant only in the

Table 3. Multivariable regression analysis of fetal brain measurements

Outcome	Predictor	B	SE	95% CI	t	p
VP	Hypothyroid antibody+	0.299	0.278	-0.251 to 0.850	1.078	0.283
VP	Hypothyroid antibody−	-0.081	0.297	-0.670 to 0.508	-0.273	0.786
NF	Hypothyroid antibody+	-0.224	0.191	-0.602 to 0.154	-1.176	0.242
NF	Hypothyroid antibody−	-0.407	0.204	-0.811 to -0.003	-1.997	0.048
CSP	Hypothyroid antibody+	0.230	0.240	-0.245 to 0.705	0.958	0.340
CSP	Hypothyroid antibody−	0.271	0.256	-0.237 to 0.779	1.056	0.293
CCL	Hypothyroid antibody+	-0.694	0.602	-1.886 to 0.498	-1.153	0.251
CCL	Hypothyroid antibody−	-0.829	0.643	-2.104 to 0.446	-1.288	0.200
CC-body	Hypothyroid antibody+	-0.241	0.268	-0.773 to 0.291	-0.898	0.371
CC-body	Hypothyroid antibody−	-0.326	0.287	-0.895 to 0.243	-1.136	0.258
Thalamus	Hypothyroid antibody+	-0.094	0.381	-0.849 to 0.660	-0.248	0.805
Thalamus	Hypothyroid antibody−	-0.744	0.407	-1.551 to 0.063	-1.828	0.070
MCA-PI	Hypothyroid antibody+	-0.334	0.097	-0.527 to -0.142	-3.441	<0.001
MCA-PI	Hypothyroid antibody−	-0.080	0.104	-0.286 to 0.126	-0.773	0.441

B: Unstandardized regression coefficient, SE: Standard error, CI: Confidence interval. All models were adjusted for gestational age, maternal BMI, and parity category. The reference group for thyroid status was the euthyroid (normal thyroid function) group. VP: Ventricular posterior width, NF: Nuchal fold thickness, CSP: Cavum septi pellucidi, CCL: Corpus callosum length, CC-body: Corpus callosum body thickness, MCA-PI: Middle cerebral artery-pulsatility index, BMI: Body mass index

antibody-positive group after adjustment. The attenuation of the association after adjustment suggests that the crude finding may have been influenced by baseline differences between groups. Compared with euthyroid pregnancies, women in the hypothyroid antibody-negative group had higher BMI values and different gravida and parity distributions, and they also tended to have lower gestational age at examination. Although BMI was included in the multivariable models, maternal obesity has been associated with chronic low-grade inflammation and altered placental function, which could theoretically influence fetal Doppler parameters (14). Therefore, residual confounding related to maternal adiposity cannot be completely excluded.

Reduced MCA-PI is often associated with a “brain-sparing” response (15) in compromised pregnancies. However, all fetuses in our cohort had normal growth parameters, suggesting that this finding may represent a subclinical or adaptive hemodynamic variation rather than overt pathology.

In contrast to the antibody-negative group, the association remained statistically significant in the antibody-positive hypothyroid group after adjustment. This finding raises the possibility that thyroid autoimmunity may contribute to changes in fetal cerebral Doppler indices beyond hypothyroidism alone; however, this interpretation should remain cautious because a euthyroid antibody-positive comparison group was not available. Maternal thyroid dysfunction and autoimmunity have been linked to endothelial dysfunction, altered vascular regulation, and inflammatory mechanisms that may theoretically affect placental function and fetal circulation. However, because MCA-PI is a surrogate marker of fetal cerebral hemodynamics rather than a direct measure of neurological function, the clinical significance of this finding remains uncertain (16,17).

Evidence regarding fetal brain structures and MCA-PI in pregnancies complicated by maternal hypothyroidism remains limited. Studies by Tugrul Ersak et al. (18) and Zhang et al. (19) have reported that maternal hypothyroidism may be associated with fetal cardiac structural and hemodynamic changes, while Paienok et al. (20) reported no significant differences in fetal cerebral circulation parameters between pregnancies complicated by thyroid disease and healthy controls. Differences between studies may be related to variations in study populations, treatment status, and gestational age at Doppler assessment. In the present study, all hypothyroid patients were receiving medical therapy; therefore, the findings should not be interpreted as the effect of overt current hypothyroidism. Rather, they may reflect prior thyroid dysfunction, treated hypothyroidism, thyroid autoimmunity, or a combination of these factors. In the present study, although routine umbilical and uterine artery Doppler assessments were within normal limits, cerebroplacental ratio (CPR) analysis and direct placental assessment were not performed. Therefore, the underlying mechanisms cannot be confirmed based on the available data.

Study Limitations

Strengths

- Prospective observational design.
- Standardized fetal neurosonographic and MCA-PI assessment.
- Blinded ultrasound examiner.
- Adjustment for gestational age, BMI, and parity.

Limitations

- Single-center design and small subgroup sizes.

- Lack of euthyroid antibody-positive group.
- Lack of CPR analysis, detailed placental assessment, and postnatal neurodevelopmental follow-up.
- Autoantibody status analyzed only as positive/negative.
- Treated hypothyroid population; untreated hypothyroidism could not be evaluated.

Conclusion

In conclusion, maternal hypothyroidism accompanied by thyroid autoimmunity was associated with lower fetal MCA-PI values in the second trimester, independent of potential confounding factors. While fetal biometric and neurosonographic parameters were not independently associated with maternal thyroid status after adjustment, the observed reduction in MCA-PI suggests a possible effect on fetal cerebral hemodynamics. Further prospective studies, including umbilical artery Doppler and direct placental assessment, are needed to clarify the underlying mechanisms and clinical significance of this association. However, these findings should be interpreted with caution, as the study was conducted at a single institution and included a sample size that may be insufficient to detect small effects, which may limit their generalizability. Larger multicenter studies are warranted to confirm these results and further elucidate the underlying mechanisms.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Institutional Ethics Committee of University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital (approval number: E-96317027-514.10, date: 16/09/2025).

Informed Consent: Written informed consent was obtained from all participants before participation in the study.

Acknowledgments

The authors would like to thank all participants and the clinical staff involved in this study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.Ö.Ç., I.T.B., Concept: H.Ö.Ç., H.E., Design: H.Ö.Ç., H.E., Data Collection or Processing: H.Ö.Ç., C.T.P., H.E., Analysis or Interpretation: H.Ö.Ç., C.T.P., I.T.B., Literature Search: H.Ö.Ç., H.E., Writing: H.Ö.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Contempré B, Jauniaux E, Calvo R, Jurkovic D, Campbell S, de Escobar GM. Detection of thyroid hormones in human embryonic cavities during the first trimester of pregnancy. *J Clin Endocrinol Metab*. 1993;77(6):1719-1722.
2. Jansen TA, Korevaar TIM, Mulder TA, White T, Muetzel RL, Peeters RP, et al. Maternal thyroid function during pregnancy and child brain morphology: a time window-specific analysis of a prospective cohort. *Lancet Diabetes Endocrinol*. 2019;7(8):629-637.
3. Bernal J. Thyroid hormones in brain development and function. 2025. In: Feingold KR, Adler RA, Ahmed SF, Anawalt B, Blackman MR, Chrousos G, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000.
4. Maraka S, Dosiou C. Subclinical hypothyroidism and thyroid autoimmunity in pregnancy: to treat or not to treat. *Endocrinol Metab Clin North Am*. 2024;53(3):363-376.
5. Shahin A, Aal NA El, El-Kelany O, Halaby A El, Elsayed A. Maternal thyroid function with placental hemodynamics and their effect on fetal and maternal outcomes. *Menoufia Medical Journal*. 2020;33(2):516-516.
6. Ralli M, Angeletti D, Fiore M, D'Aguanno V, Lambiase A, Artico M, et al. Hashimoto's thyroiditis: an update on pathogenic mechanisms, diagnostic protocols, therapeutic strategies, and potential malignant transformation. *Autoimmun Rev*. 2020;19(10):102649.
7. Türkiye Endokrinoloji ve Metabolizma Derneği. Tiroid hastalıkları tanı ve tedavi kılavuzu, 2025. [internet]. Erişim adresi: https://file.temd.org.tr/Uploads/publications/guides/documents/tiroid2025_11042025.pdf
8. Paladini D, Malinger G, Birnbaum R, Monteagudo A, Pilu G, Salomon LJ, et al. ISUOG Practice Guidelines (updated): sonographic examination of the fetal central nervous system. Part 2: performance of targeted neurosonography. *Ultrasound Obstet Gynecol*. 2021;57(4):661-671. Erratum in: *Ultrasound Obstet Gynecol*. 2022;60(4):591.
9. Malinger G, Paladini D, Haratz KK, Monteagudo A, Pilu GL, Timor-Tritsch IE. ISUOG Practice Guidelines (updated): sonographic examination of the fetal central nervous system. Part 1: performance of screening examination and indications for targeted neurosonography. *Ultrasound Obstet Gynecol*. 2020;56(3):476-484. Erratum in: *Ultrasound Obstet Gynecol*. 2022;60(4):591.
10. Bhide A, Acharya G, Baschat A, Bilardo CM, Brezinka C, Cafici D, et al. ISUOG Practice Guidelines (updated): use of Doppler velocimetry in obstetrics. *Ultrasound Obstet Gynecol*. 2021;58(2):331-339.
11. Torun R, Golbasi H, Saglam C, Tuncer Can S, Gercik I, Ankara Aktas H, et al. Evaluation of the fetal brain in maternal hypothyroidism and thyroid autoantibody positivity: a prospective case-control study. *J Clin Med.* 2025;14(7):2204.
12. Lee SY. No significant impact of levothyroxine treatment of maternal subclinical hypothyroidism on brain morphology in adolescence: insight from long-term follow up of controlled antenatal thyroid screening (CATS) study. *Ann Transl Med*. 2026;14(2):23.

13. Korevaar TIM, Muetzel R, Medici M, Chaker L, Jaddoe VW V, de Rijke YB, et al. Association of maternal thyroid function during early pregnancy with offspring IQ and brain morphology in childhood: a population-based prospective cohort study. *Lancet Diabetes Endocrinol*. 2016;4(1):35-43.

14. Louwen F, Kreis NN, Ritter A, Yuan J. Maternal obesity and placental function: impaired maternal–fetal axis. *Arch Gynecol Obstet*. 2024;309(6):2279-2288.

15. Baschat AA, Hecher K. Fetal growth restriction due to placental disease. *Semin Perinatol*. 2004;28(1):67-80.

16. Sá MI, Illa M, Guedes-Martins L. Doppler assessment of the fetal brain circulation. *Diagnostics (Basel)*. 2026;16(2):214.

17. Bao Z, Li Y, Xue T, Liu Y, Yan J, Wang X, et al. Pathological features of the placenta in hypothyroidism during pregnancy: a population-based retrospective cohort study in Chinese population. *Front Endocrinol (Lausanne)*. 2025;16:1671641.

18. Tugrul Ersak D, Oluklu D, Uyan Hendem D, Turgut E, Göncü Ayhan Ş, Kara Ö, et al. The assessment of fetal cardiac output in maternal hypothyroidism under levothyroxine treatment. *Echocardiography*. 2022;39(11):1434-1438.

19. Zhang Y, Zhang L, Zhao W, Li N, Chen G, Ge J, et al. Cardiac structural and functional remodeling in the fetuses associated with maternal hypothyroidism during pregnancy. *J Matern Fetal Neonatal Med.* 2023;36(1):2203796.

20. Paienok OS, Protsiuk RG, Paienok A V, Zadorozhna B V, Hrytsyshyn BR, Ihnatovych SV. The association of maternal thyroid function with placental hemodynamics during pregnancy. *Mižnarodnij endokrinologičnij žurnal*. 2024;20(4):323-327.